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### **Remarks/Arguments**

Applicants respectfully request entry of the above amendment after final rejection and reconsideration of the subject application, particularly in view of the above amendment after final rejection and the following remarks. Applicants respectfully urge that there is no additional fee for this amendment because the number of independent claims remains unchanged and the total number of claims has been reduced.

Applicants wish to thank the Examiner for granting a telephone interview with the undersigned subsequent to the issuance of the final Office Action. Applicants also wish to acknowledge the helpful comments provided by the Examiner in clarifying the issues related to the rejection of the subject application.

Applicants have amended Claim 1 of the subject application by incorporating all of the limitations of Claim 2, as a result of which Claim 2 has been canceled. In addition, Applicants have amended Claim 10 of the subject application by incorporating all of the limitations of Claim 11, as a result of which Claim 11 has been canceled. Applicants respectfully urge that this amendment incorporates no new matter into the claims and raises no new issues which would require further search and/or consideration by the Examiner.

The invention claimed by Applicants is a method for introducing and stabilizing heterologous and recombinant genes in a thermophilic host in which a malate dehydrogenase gene in the thermophilic host, which gene affects host growth rate, is inactivated or removed from the thermophilic host. The result is a modified thermophilic host having a reduced growth rate. A DNA fragment of interest is then inserted into the modified thermophilic host together with an intact or restored malate dehydrogenase gene, as a result of which the host growth rate increases, thereby enabling detection or confirmation of successful transformation using plasmid vectors and integration of the DNA fragment into a chromosome of the thermophilic host. The malate dehydrogenase gene (*mdh*), when rendered inactive in the *Thermus* sp., results in a low growth rate phenotype, i.e. a “sick” colony phenotype. The initial higher growth rate phenotype, i.e. “healthy” phenotype, is restored by introduction/transformation of a plasmid, integration vector or DNA fragment containing an intact *mdh* gene as well as a gene of interest. In this manner the presence of the gene of interest in the thermophilic host can be confirmed. Applicants respectfully urge that the prior art relied upon by the Examiner as the basis for rejection of the subject application neither teaches nor suggests a method in which a malate dehydrogenase gene of a thermophilic host is used to confirm the successful insertion of a gene of interest into the thermophilic host based upon the modification

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and subsequent restoration of growth rate through deactivation or removal followed by reactivation or restoration of the malate dehydrogenase gene as claimed by Applicants.

Claims 1-3, 5, 10 and 11 have been rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. Applicants respectfully traverse this rejection. The Examiner alleges that the claims contain subject matter which is not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. In particular, the Examiner indicates that the limitation of “inactivating or deleting a characteristic gene defining host growth rate” was not described in the application as originally filed, notwithstanding the fact that the specification identifies the *mdh* gene as a gene which affects the growth rate of a thermophilic host. Applicants understand the Examiner’s position to be that because the specification contains no general statement regarding the step of deleting or inactivating genes which affect growth rate, there is no support for the breadth of the claims reciting Applicants’ claimed invention and, thus, the claims are not allowable. Applicants respectfully urge that this rejection is overcome as a result of the above amendment. In particular, the invention as originally claimed and as described in the application (Page 2, lines 8-11) was a method which

encompassed a characteristic gene defining *any detectable host characteristic*. Examples of such genes were indicated to be the malate dehydrogenase (*mdh*) gene, the phytoene dehydrogenase gene and the beta-galactosidase gene (Page 2, lines 11-13). Applicants have amended the claims so as to limit the scope of the claimed invention to the use of the malate dehydrogenase gene, an example of the use of which is clearly described in the application. Accordingly, Applicants respectfully urge that the subject matter of the amended claims is described in a manner which satisfies the written description of 35 U.S.C. 112, first paragraph and, thus, respectfully urge that the above amendment overcomes this rejection.

Claims 1, 3, 5 and 10 have been rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. Applicants respectfully traverse this rejection. The Examiner alleges that the claims contain subject matter which is not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. In particular, the Examiner indicates that the rejection is based on the Guidelines for the Examination of Patent Applications under 35 U.S.C. 112, first paragraph, "Written Description" published in the Federal Register (Volume 66, No. 4, pp 1099-1111). More particularly, the Examiner indicates that the current claims are genus claims in terms

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of a method comprising inactivating or deleting any gene defining a host growth rate from a thermophilic host or utilizing a *Thermus* strain comprising an inactivated or deleted characteristic gene defining a strain growth rate and that the single example of the *mdh* gene as a gene affecting the growth rate of a thermophilic host is not sufficient disclosure to encompass any gene defining host growth rate. As previously indicated, Applicants have amended the claims so as to limit the scope of the claims to a single disclosed species, i.e. malate dehydrogenase genes. Applicants further respectfully urge that the specification clearly describes the use of the malate dehydrogenase gene in the method of the invention claimed by Applicants beginning at Page 9, line 7 of the subject application. Accordingly, Applicants respectfully urge that the amendment of the claims to require the use of the malate dehydrogenase gene overcomes this rejection under 35 U.S.C. 112, first paragraph.

Claims 1-3 and 5 have been rejected under 35 U.S.C. 102(a) as being anticipated by Kayser et al., J. Bacteriol., Vol. 183, No. 5, pp. 1792-1795 (Mar. 2001) (hereinafter "the Kayser et al. reference"). This rejection is respectfully traversed. The subject application has a filing date of 28 February 2002, which filing date is less than one year following the date of publication of the Kayser et al. reference. In addition, by virtue of the amendment of the inventorship of the subject application as a result of the cancellation of certain of the claims by a previous amendment, *all of*

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*the inventive entities of the Kayser et al. reference and the subject application are identical*, a fact which the Examiner acknowledged overlooking during the course of the aforementioned telephone interview. Applicants respectfully urge that, because the Kayser et al. reference has a publication date less than one year preceding the filing date of the subject application, and because there is identity between the authors of the Kayser et al. reference and the inventors of the invention claimed in the subject application, the Kayser et al. reference is not prior art properly cited against the subject application. MPEP § 706.02(a)*III* states that, for 35 U.S.C. 102(a) to apply, the reference must have a publication date earlier in time than the effective filing date of the application, *and must not be applicant's own work*. Because the cited reference is Applicants' own work, and because the reference has a publication date less than one year prior to the effective filing date of the subject application, Applicants respectfully urge that the Kayser et al. reference does not anticipate the invention claimed by Applicants in the manner required by 35 U.S.C. 102(a).

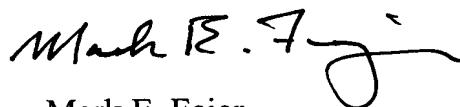
### **Conclusion**

Applicants intend to be fully responsive to the outstanding Office Action. If the Examiner detects any issue which the Examiner believes Applicants have not addressed in this response, Applicants urge the Examiner to contact the undersigned.

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Applicants sincerely believe that this patent application is now in condition for allowance and, thus, respectfully request early allowance.

Respectfully submitted,

A handwritten signature in black ink, appearing to read "Mark E. Fejer", with a stylized flourish at the end.

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